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Potential food allergens in medications

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Activity Objectives

1. To describe which food-derived substances are used as pharmaceutical excipients in which medications.
2. To review published data regarding the safety of administration of these medications to recipients with food allergy.
3. To prescribe these medications to most patients with food allergies.
4. To investigate potential allergy to the food component if a particular patient has had an apparent allergic reaction to a medication containing it.

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Excipients are substances in pharmaceuticals other than the active ingredients. Some excipients are foods or substances derived from foods, raising the possibility that these substances would pose a hazard to patients with food allergy. This review describes which food-derived substances are used as pharmaceutical excipients in which medications and reviews published data regarding the safety of the administration of these medications to recipients with food allergy. Such reactions are rare, usually because the amount of food protein is not present in a large enough quantity to elicit a reaction. When a food protein appears as an unintentional contaminant, the amount, if any, that is present might be variable and might elicit reactions only from some lots of medication or only in some patients. In most circumstances these medications should not be routinely withheld from patients who have particular food allergies because most will tolerate the medications uneventfully. However, if a particular patient has had an apparent allergic reaction to the medication, potential allergy to the food component should be investigated. (J Allergy Clin Immunol 2014;133:1509-18.)

Key words: *Food allergy, medication allergy, vaccine allergy*

Abbreviations used
IIV: Inactivated influenza vaccine
ILE: Intravenous lipid emulsion
LAIV: Live attenuated influenza vaccine
TPN: Total parenteral nutrition

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Excipients are all of the substances found in pharmaceuticals other than the active ingredients. These substances are added to "aid the manufacturing process, to protect, support or enhance stability, or for bioavailability or patient acceptability."[1] Some pharmaceutical excipients are foods or, more often, substances derived from foods, raising the possibility that these substances would pose a hazard to patients with food allergy.[2] The purpose of this publication is to describe which food-derived substances are used as pharmaceutical excipients in which medications (Table I)[3-171] and to review published data regarding the safety of the administration of these medications to recipients with food allergy.

Virtually all food allergens that generate IgE-mediated responses are proteins. In some cases the food excipients in medications are in fact proteins and thus capable of being allergenic. The amount and nature of (eg, how thoroughly hydrolyzed) these proteins might influence their allergenic potential. However, in many other cases the food excipient in the medication is a fat or carbohydrate and thus would not be expected to be allergenic. In these cases the excipient would have

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TABLE I. Potential food allergens in medicines

Food	Excipients	Drugs
Egg	Egg protein/ovalbumin	• Interferon Alfa-n3* • Probiotics[143] • Vaccines[3]: influenza* (IIV,[31-58] LAIV) MMR*[4-30] Rabies (PCEC) Yellow fever*
	Egg lecithin/ phospholipids	• Emulsions: Clevidipine* Fat emulsions[62,63] Propofol*[64-81] Tablets: Diphenhydramine Denofibrate Ibuprofen Multivitamin Rosiglitazone • Verteporfin injection[82]
Fish	Protamine	• Protamine injection*[83-91] • NPH insulin
	Fish oil	• Fish oil supplements[94] • Some multivitamins
Gelatin	Gelatin	• Many capsules and tablets[97,98] • Benzocaine oral gel • Chloral hydrate suppositories[99] • Corticotropin repository injection • Erythropoietin[100] • Hemostatic sponges[101,102] • Nicotine chewing gum • Plasma volume expanders[103-120] • Sulfur colloid injection[121] • Vaccines[3]: Influenza (Fluzone,[135] FluMist*) Japanese encephalitis[125,127,133] MMR*[95,96,122,123,126,128,130,132,134,136,137] MMRV* Rabies (RabAvert)* Tick-borne encephalitis[131] Typhoid vaccine, live oral Varicella*[123,124,129,130,138] Yellow fever* Zoster*
Milk	Casamino acids	• Vaccines[104,141]: DTaP (Daptacel) DTaP-IPV/Hib (Pentacel) Meningococcal (Menomune) Pneumococcal (PCV13 – Prevnar 13) Td (Tenivac) Tdap (Adacel)
	Casein	• Cefditoren tablets* • Miconazole tablets* • Probiotics[142] • Vaccines[140,141]: DTaP (Infanrix) DTaP+HepB+IPV (Pediarix) DTaP+IPV (Kinrix) Tdap (Boostrix) Typhoid (Vivotif)
	Cow's milk	• Some psyllium solutions • Tums Smoothies tablets
	Lactalbumin	• OPV[143]
	Lactose[144]	• Many tablets, capsules, granules, and lyophilized powders[145] • Some psyllium solutions • DPIs: device name (drug name/s)[146-148] Aerolizer (Foradil)* Diskus (Advair, Flovent, Ventolin)* Flexhaler (Pulmicort)* HandiHaler (Spiriva)* Neohaler (Arcapta)* Pressair (Tudorza)* Rotahaler (Tiova) Turbuhaler/Turbohaler (Bricanyl, Oxis*, Pulmicort*, Symbicort*) Twisthaler (Asmanex)*
	Lactulose	• Lactulose solution[149]
Peanut	Peanut oil	• Dimercaprol injection* • Progesterone capsules* • Valproic acid capsules
Pine nut	Rosen	• Fluoride tooth varnish[150]
Sesame	Sesame oil	• Dronabinol capsules* • Estradiol injection • Fluphenazine decanoate injection • Haloperidol decanoate injection • Nandrolone decanoate injection • Progesterone injection* • Testosterone injection
Shellfish	Glucosamine	• Dietary supplements for arthritis[151-156]
	Iodine	• Radiocontrast media[157]
Soy	Soy lecithin	• MDIs[161-166] Atrovent Combivent*
	Soy oil	• Emulsions: Clevidipine* Fat emulsions[158-160,167-171] Propofol*[64-81]
	Soy phosphatidylcholine	• Amphotericin B liposome • Doxorubicin liposome
	Soybean	• Tums Smoothies tablets

Note that hundreds of nutritional supplements and homeopathic remedies not regulated by the US Food and Drug Administration also contain food ingredients.
DPI, Dry powder inhaler; *MDI*, metered-dose inhaler; *MMR*, measles-mumps-rubella; *PCEC*, purified chick embryo cell.
*The package insert lists food allergy as a warning or contraindication.

to be contaminated with protein for an allergen to be present. This type of contamination might well be random or variable. This variability in the amount and nature of food protein present in medications by design or by accident means that there could be great lot-to-lot variability in the presence of these proteins. Individual patients would also be expected to vary quite widely in susceptibility to allergic reactions with exposure to these food proteins in medications, depending on the amount of IgE antibody generated against the particular food allergen and particular epitopes on the food allergen.

EGG

Egg protein/ovalbumin

Vaccines. Measles, mumps, and purified chick embryo cell rabies vaccines are grown in chick embryo fibroblast cultures and

contain negligible or no egg protein. Thus despite some discussion in the warnings sections of the package inserts, measles-mumps-rubella and purified chick embryo cell rabies vaccine can be administered to recipients with egg allergy in the usual manner.[3-30,173]

Egg protein is present in higher amounts in influenza and yellow fever vaccines and in theory could cause reactions in patients with egg allergy. However, in 27 published studies, collectively, 4172 patients with egg allergy received 4729 doses of inactivated influenza vaccine (IIV) with no cases of anaphylaxis, including 513 with severe allergy who uneventfully received 597 doses.[31-58] This is likely due to the very low amount of egg protein present in these vaccines.[3,59-61] The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices and the American Academy of Pediatrics' Committee on Infectious Diseases recommend that persons with egg allergy receive IIV as a single dose without prior vaccine skin testing and be observed for 30 minutes afterward for any possible allergic reaction.[174,175] If the reaction to the ingestion of eggs is hives only, the vaccine can be administered in a primary care setting, whereas if the reaction to the ingestion of eggs is more severe, the vaccine should be administered in an allergist's office. Two new IIVs not grown in eggs have been approved for patients 18 years and older: Flucelvax,[176] which is prepared from virus propagated in cell culture, and Flublok,[177] which consists of recombinant hemagglutinin proteins produced in an insect cell line. For patients with egg allergy 18 years of age and older, either egg-based or egg-free IIV can be used. Live attenuated influenza vaccine (LAIV) also contains a very low amount of egg protein.[3] Because there are no published studies on the safety of LAIV in recipients with egg allergy, guidelines recommend the use of IIV in these patients,[174,175,178] although LAIV would be expected to have a safety profile similar to that of IIV.

Per the yellow fever vaccine package insert,[179] recipients with egg allergy should be skin tested with the vaccine before administration. If results are negative, the vaccine can be given in the usual manner, but the patient should be observed for 30 minutes afterward. If the vaccine skin test result is positive, the vaccine can be administered in graded doses under observation.

Egg lecithin/phospholipids

Lecithin is a fatty substance occurring in animal and plant tissues composed of phosphoric acid, choline, fatty acids, glycerol, glycolipids, triglycerides, and phospholipids. Commercial sources of lecithins for use in pharmaceutical agents include soybean oil and egg yolk, and these products contain some residual protein,[180] although reports of allergic reactions to them are rare and largely unsubstantiated, and thus patients with soy and egg allergy need not avoid them.

Intravenous lipid emulsions. Some intravenous lipid emulsions (ILEs) contain 1.2% egg yolk phospholipids.[62] There is a single case report of a child having diffuse pruritus after 14 days of treatment with ILEs who had IgE antibody to egg yolk, but no testing with the ILEs was performed.[63] Most purported allergic reactions to ILEs are in relation to soy, as below.

Propofol. Propofol is an intravenous sedative-hypnotic agent used in anesthesia. It is formulated in a fat emulsion containing soybean oil (100 mg/mL) and egg lecithin (12 mg/mL).[181,182] There are numerous reports of urticarial or anaphylactic reactions to propofol.[64-81] Although most reports of anaphylaxis to propofol have occurred in patients without egg allergy, 2 reports have implicated egg as a possible allergen,[73,77] although no testing was done to support this contention. Furthermore, the vast majority of patients with egg allergy receive propofol uneventfully.[81] Some reports of apparent allergic reactions to propofol have included positive immediate-type skin test results or serum specific IgE antibody assays, suggesting a possible IgE-mediated mechanism.[66,70-72,74,78,80] Intradermal skin test concentrations as high as 1 mg/mL have been reported to be nonirritating.[71] However, the conclusion that cases of anaphylaxis are due to an IgE-mediated reaction to propofol are complicated by several factors, including that many patients have had such reactions after receiving the drug for the first time and that many such cases have occurred with simultaneous administration of other drugs that can cause or worsen anaphylaxis, including muscle relaxants and opioid analgesics.[71] Thus although it is clear that propofol can cause anaphylactic reactions, the mechanism of these reactions is unclear and appears unrelated to egg allergy.

Verteporfin. There is a single case report of anaphylaxis after infusion of verteporfin used to treat macular degeneration.[82] The medication contains egg phosphatidylglycerol, but there is no mention of egg allergy in the patient.

FISH

Protamine

Protamines are small proteins involved in sperm biology.[183] Protamine for pharmaceutical use is isolated from salmon testes and is used to reverse the effects of heparin and complexed to some insulins to delay absorption.[184] Urticarial and anaphylactic reactions to protamine have been reported.[83-91] Some reports have suggested that these reactions might be due to cross-reactions with other fish proteins,[83,84,88] although no testing was done to support this contention. Furthermore, ELISA inhibition studies with sera from patients with salmon allergy showed no inhibition with protamine, and serum from a patient with protamine allergy showed no inhibition with salmon.[92] Also, most patients with fish allergy tolerate protamine uneventfully.[85] Some reports of apparent allergic reactions to protamine have included positive immediate-type skin test or serum specific IgE antibody assay results, suggesting a possible IgE-mediated mechanism.[86] However, results of protamine skin tests and serum specific IgE antibody assays correlate poorly with each other, and both are poorly correlated with reactions to protamine; that is, most patients with positive test results do not react to protamine, and most patients with reactions have negative test results.[87,93] Thus although it is clear that protamine can cause anaphylactic reactions, the mechanism of these reactions is unclear and appears unrelated to fish allergy, and thus patients with fish allergy need not avoid protamine.

Fish oil

Fish oils are generally highly refined and should not contain fish protein.[185] Patients with fish allergy have been challenged

with fish oils and show no reaction.[94] Thus patients with fish allergy need not avoid fish oil.

GELATIN

Gelatin is produced by partial hydrolysis of collagen extracted from connective tissues of animals, such as cows or pigs. Thus it contains potentially allergenic protein fragments. Bovine and porcine gelatins are extensively cross-reactive.[95,96,186,187] There are many well-documented cases of IgE-mediated anaphylactic reactions to the gelatin-containing products listed below, and patients with gelatin allergy should generally avoid them. Most reactions involve parenteral exposure. Oral exposure to gelatin-containing capsules has only rarely been reported to cause reactions, and patients with gelatin allergy are generally able to tolerate these.

Capsules

Despite their widespread use, there are only 2 case reports of allergic reactions to gelatin capsules.[97,98]

Suppositories

Anaphylaxis in 10 children to gelatin-containing chloral hydrate rectal suppositories has been reported, with all of these children having serum specific IgE to gelatin.[99]

Erythropoietin

There is a single case report of a patient who had anaphylaxis after infusion of an erythropoietin preparation containing gelatin but who tolerated a non–gelatin-containing preparation of the same medication.[100] She was subsequently found to have increased specific IgE levels to gelatin.

Hemostatic sponges

Gelfoam (Pfizer, New York, NY) is in absorbable gelatin sponge prepared from purified porcine skin applied to bleeding surfaces as a hemostatic agent.[188] Two cases of intraoperative anaphylaxis have been attributed to allergic reactions to this material, and this hypothesis was supported by increased serum specific IgE levels to gelatin.[101,102]

Plasma volume expanders

Several gelatin solutions are used outside the United States as colloid plasma volume expanders, including succinylated gelatin or modified fluid gelatin, urea-linked gelatin or polygeline, and oxypolygelatin.[189] There are many reports of anaphylaxis to the infusion of these materials,[103-120] including fatalities.[108,110] The rate of such reactions is reported to be 0.075% of units infused.[112] Many of these reports have demonstrated positive immediate-type allergy skin test results to the gelatin solutions,[103,104,112,115,117,118] and 1 report demonstrated positive basophil activation as well.[118] Gelatin solution infusions can induce histamine release in a small percentage of healthy subjects without prior exposure, although typically without clinical consequence or causing hives only, suggesting that some reactions might be due to direct mast cell degranulation.[105,109,111]

TABLE II. Gelatin content of US vaccines, 2014

Vaccine	Gelatin content
Influenza (Fluzone [trivalent only]; Sanofi Pasteur, Lyon, France)	250 μg per 0.5-mL dose
Influenza (FluMist; MedImmune Vaccines, Gaithersburg, Md)	2,000 μg per 0.2-mL dose
Measles, Mumps, Rubella (MMRII; Merck, Whitehouse Station, NJ)	14,500 μg per 0.5-mL dose
Measles, Mumps, Rubella, Varicella (ProQuad, Merck)	11,000 μg per 0.5-mL dose
Rabies (RabAvert; Novartis, Emeryville, Calif)	12,000 μg per 1.0-mL dose
Typhoid Vaccine Live Oral Ty21a (VIVOTIF; Berna, Coral Gables, Fla)	Capsule
Varicella (VARIVAX, Merck)	12,500 μg per 0.5-mL dose
Yellow Fever (YF-VAX, Sanofi Pasteur)	7,500 μg per 0.5-mL dose
Zoster (ZOSTAVAX, Merck)	15,580 μg per 0.65-mL dose

Sulfur colloid injection

There is a single case report of an anaphylactic reaction after the infusion of a technetium sulfur colloid stabilized with gelatin; however, no testing was done to determine the potential allergen.[121]

Vaccines

A number of (mostly live viral) vaccines contain gelatin as a stabilizer (Table II).[3] There are many well-documented cases of anaphylaxis to gelatin-containing vaccines in recipients subsequently determined to have serum specific anti-gelatin IgE.[95,96,122-135] Most such reactions have occurred after injection of vaccines that contain milligram quantities of gelatin, namely measles-mumps-rubella,[95,96,122,132,134] varicella,[123,124,129] and Japanese encephalitis[125,127,133] vaccines. Some patients with gelatin allergy tolerate the ingestion of gelatin yet have systemic allergic reactions to gelatin injected in a vaccine,[95] presumably because digestion allows for the proteins to be broken down into fragments too small to remain allergenic before absorption. However, patients with histories of reactions to the ingestion of gelatin confirmed by skin tests or specific IgE assays to gelatin should undergo vaccine skin testing before receipt of gelatin-containing vaccines.[3] Most patients with gelatin allergy generate IgE antibodies to a 10-amino-acid epitope on the α-2 chain of type I collagen, a sequence not found on human type I collagen.[190,191] The incidence of gelatin allergy appears to be higher in Japan,[136] perhaps because of an HLA type (DR 9) common in Japanese subjects.[192] In Japan vaccine manufacturers removed gelatin or changed to a less allergenic (more thoroughly hydrolyzed) gelatin in vaccines, after which there was a dramatic decrease in reports of anaphylaxis associated with these vaccines.[137,138] Vaccines in many other countries, including the United States, continue to contain gelatin (Table II).

MILK

Reports of allergic reactions to pharmaceuticals in patients with milk allergy are rare, and in general, such patients need not avoid the products below.

Casamino acids

Vaccines. A series of 8 patients with high-level milk allergy has been reported who had anaphylactic reactions after receiving

DTaP or Tdap vaccines.[140] The growth media for these vaccines contain casamino acids derived from casein, and nanogram quantities of casein are present in the vaccines, which might be sufficient to trigger reactions in exquisitely sensitive patients. Other authors have challenged this association and noted no safety signal in the Vaccine Adverse Event Reporting System database among patients with milk allergy receiving these vaccines.[141]

Casein

Probiotics. There is a single case report of an anaphylactic reaction to a probiotic in a child with milk and egg allergy.[142] Cow's milk is the culture medium for most probiotics. The child had a positive skin prick test result with the suspect probiotic, and several probiotics analyzed contained milk and, in some cases, egg protein.

Lactalbumin

Vaccines. A series of 4 children with milk allergy has been reported who had immediate-type allergic reactions after oral polio vaccine.[143] The Italian manufacturer of the vaccine listed α-lactalbumin as an ingredient, which was confirmed by using ELISA. Patient IgE directed against the vaccine was partially inhibited by α-lactalbumin.

Lactose

Lactose is milk sugar purified from cow's milk. Pharmaceutical-grade lactose is generally thought to be free of contaminating milk proteins. Twenty-four children with positive double-blind, placebo-controlled food challenge results to milk ingestion and positive skin prick test responses and serum specific IgE assay results to milk had negative skin test and oral challenge results with lactose.[144] Immunoblotting did not reveal the presence of any protein in the lactose preparations. Nonetheless, on rare occasions, lactose can be contaminated by milk proteins, as below.

Methylprednisolone injections. A series of 2 patients with high-level milk allergy has been reported who had urticarial reactions after receiving lactose-containing methylprednisolone injections.[145] The patients had positive immediate-type skin test results to the suspect medication but not to a lactose-free preparation of methylprednisolone. Assay of the lactose-containing methylprednisolone revealed nanogram quantities of β-lactoglobulin.

Dry powder inhalers. Most dry powder inhalers containing medications to treat asthma or chronic obstructive pulmonary disease contain lactose to improve drug delivery and to impart taste to indicate dose delivery.[146] A child with severe milk allergy has been reported who had chest tightness and a decrease in FEV_1 and blood pressure immediately after an inhalation from a dry powder inhaler containing lactose.[146] The patient had a positive immediate-type skin test result to the suspect lot of medication but not to a different lot. Some milk proteins were detected in some other dry powder inhalers. Similar reactions have been reported in 1 other child with milk allergy[147] and 1 other adult with milk allergy.[148] This is apparently quite a rare phenomenon given the large number of children with milk allergy who use lactose-containing dry powder inhalers uneventfully.

Lactulose

Lactulose is a synthetic nondigestible disaccharide produced by isomerization of lactose used to treat constipation. There is a single case report of an apparent allergic reaction in a child with milk allergy after ingestion of lactulose syrup, but no testing was done to demonstrate that the reaction was due to any milk protein that could possibly have been contaminating the medication.[149]

PEANUT

Peanut oil

The package inserts for dimercaprol for injection, progesterone capsules, and valproic acid capsules list peanut oil as an ingredient, and the former 2 drugs also list peanut allergy as a precaution. However, there are no reports of allergic reactions to peanut oil in these medications, presumably because pure peanut oil is not allergenic.[193]

PINE NUT

Rosin

Rosin, also called colophony, is a solid form of resin obtained from pine tree stumps. Some fluoride tooth varnish contains rosin.[150] Some patients with allergy to pine nuts have questioned whether it would be safe to use pine rosin–containing tooth varnish. Although colophony is a well-known cause of allergic contact dermatitis, it would not be expected to contain pine nut allergens, and there are no reports of immediate-type hypersensitivity reactions to rosin in patients with pine nut allergy.

SESAME SEED

Sesame oil

A number of medications contain sesame oil as an ingredient, and some list allergy to sesame oil as a contraindication. Food-grade sesame oil is typically used unrefined for its flavor,[194] and there are rare reports of patients with allergic reactions to sesame oil because of protein contamination.[195] However, refined pharmaceutical-grade sesame oil would not be expected to be allergenic unless it was contaminated by residual protein, and there are no reports of allergic reactions to sesame oil–containing medications.

SHELLFISH

Glucosamine

Glucosamine is an amino sugar derived from the shells of shellfish. Potentially allergic skin reactions have been reported in association with the ingestion of glucosamine.[151,152] There is a single case report of an urticaria/angioedema reaction to the ingestion of glucosamine in a patient with no mention of shellfish allergy.[153] A skin prick test response was negative but intradermal test results were positive in the patient but negative in 10 control subjects, and an ELISA result was negative. Another report describes an asthma exacerbation after glucosamine ingestion, but there was no mention of shellfish allergy, and no testing was performed.[154] On the other hand, 6 patients with documented shellfish allergy by history and skin testing underwent glucosamine skin tests, results of all of which were negative, and oral challenges, all of which were uneventful.[155] Another study describes 15 patients with shrimp allergy who

consumed shrimp-derived glucosamine without a reaction.[156] Thus, shellfish-allergic patients need not avoid glucosamine.

Iodine

Both shellfish and radiocontrast media contain iodine, and both can cause anaphylactic reactions. However, anaphylactic reactions to shellfish are IgE mediated, with allergic antibodies directed against protein constituents, whereas anaphylactic reactions to radiocontrast media are not IgE mediated but rather related to osmolarity. Neither shellfish nor radiocontrast reactions are related to iodine directly, and there is no association between these 2 reactions. Although atopy in general might slightly increase the risk of reactions to radiocontrast media, shellfish allergy does not pose any particular risk.[157] Thus patients with shellfish allergy do not require special precautions when receiving radiocontrast media unless they have had a prior reaction to radiocontrast media itself.

SOY

Reports of allergic reactions to pharmaceuticals in patients with soy allergy are rare, and in general, such patients need not avoid the products below.

Soy lecithin

As described above, the term lecithin describes certain fatty substances derived for pharmaceutical use of soybean oil and egg yolk.[180] Soy lecithin can contain residual soy protein,[158-160] although reports of allergic reactions are rare and largely unsubstantiated, and thus patients with soy allergy need not avoid soy lecithin.

Metered-dose inhalers. There are a few reports of asthma exacerbations or other potentially allergic reactions in association with the use of metered-dose inhalers containing soy lecithin.[161-166] In some of these reports, the authors have speculated that the reactions might have been due to soy allergy, although none of the reports describe any testing to investigate this possibility.

Soy oil

Intravenous lipid emulsions (ILEs). Most ILEs used for total parenteral nutrition (TPN) contain soy oil as a source of fat. There have been a small number of urticarial or anaphylactic reactions reported in association with the infusion of this material.[167-172] In some cases the reactions were reproducible,[167,169] but in other cases they were not.[169,170] In most cases skin tests to the suspect ILE were not performed, but when they were, the results were negative, suggesting the reactions were not IgE mediated.[167,169,172] TPN regimens typically include, along with ILEs, solutions containing amino acids and vitamins. There are a number of reports of urticarial or anaphylactic reactions to TPN regimens that either did not include ILEs[196,197] or in which the ILE component was tolerated but some other component appeared to be responsible for the reaction.[198-200] Some samples of soybean oil have been demonstrated to contain very low but measurable quantities of soy proteins,[158,159] but immunoblotting with sera from patients with soy allergy did not show any IgE binding.[159] Thus although it is clear that TPN with or without ILEs can rarely cause anaphylactic reactions, the mechanism of these reactions is unclear and appears unrelated to soy allergy.

Soy phosphatidylcholine

Liposomal amphotericin B. Amphotericin B is available in a liposomal preparation in which the principal constituent of the liposome is soy phosphatidylcholine. Anaphylactic reactions to the infusion of this preparation have been reported,[201-209] including 1 death.[206] Some of these patients tolerated the subsequent infusion of a nonliposomal preparation of amphotericin, strongly suggesting that something other than the drug itself was the cause.[201,207,208] None of the reports mention soy allergy in the patients or as a speculated mechanism.

SUMMARY

Certain substances derived from foodstuffs are used as excipients in drugs and vaccines for their pharmaceutical properties. Some of these food-derived excipients contain food proteins either intentionally or unintentionally as contaminants. As such, patients who have IgE antibodies directed against these food proteins are theoretically at risk for allergic reactions when exposed to the food proteins in the medications. However, such reactions are quite rare, usually because the amount of food protein is not present in a large enough quantity to elicit a reaction or because the particular protein is not a common allergen. When the food protein appears as an unintentional contaminant, the amount of protein, if any, that is present might be variable and might elicit reactions only from some lots of medication that happen to contain more of the food protein or illicit reactions only in patients who are exquisitely sensitive or happen to have IgE antibodies directed against a particular epitope in the contaminating protein. In most circumstances these medications should not be routinely withheld from patients who have particular food allergies because the overwhelming majority will tolerate the medications uneventfully. However, if a particular patient has had an apparent allergic reaction to the medication, allergy to the food component should be investigated as a possible cause. Even in this circumstance (ie, an allergic reaction to a medication in a patient allergic to a particular food and the presence of the food protein in the medication), the food protein would still have to be demonstrated to be causal by using appropriate testing because other allergens present in the medication could have been the cause or the medication might be capable of non–IgE-mediated mast cell degranulation.

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